Exhibit 1

Certificate of Service

I hereby certify that this correspondence is being filed with the U.S. Patent and Trademark Office via EFS-Web on 10/23, 2006.

Autrey Brown

Autrey Brown

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re: Application of Philip J. Scarpace and Gang Li	Confirmation Number: 5010
Application Number: 10/822,613	Examiner: Salvoza, M. Franco G.
Filed: April 12, 2004	Group Art Unit: 1648
For: rAAV VECTOR-BASED PRO-OPIOMELANOCORTIN COMPOSITIONS AND METHODS OF USE	Atty. Dkt. No.: **36689.26** (formerly WMA 4300.015400)

STATUTORY DECLARATION OF PHILIP J. SCARPACE AND GANG LI UNDER 37 C. F. R. § 1.131

Mail Stop After Final
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

WE, PHILIP J. SCARPACE AND GANG LI, HEREBY DECLARE AS FOLLOWS:

1. We are co-inventors of the subject matter disclosed and claimed in the captioned patent application.

2. I, Philip J. Scarpace, Ph.D., am a Professor in the Department of Pharmacology and Therapeutics at the University of Florida, College of Medicine, Gainesville, FL, and in the Department of Geriatric Research, Education and Clinical Center, Malcom Randall Veterans Affairs Medical Center, Gainesville, FL. I am citizen of the United States and currently reside in Gainesville, FL. A copy of my *curriculum vitae* is attached hereto as **Exhibit A**.

3. I, Gang Li, Ph.D., am a Postdoctoral Associate in the Department of Pharmacology and Therapeutics at the University of Florida, College of Medicine, in Gainesville, FL. I am a citizen of China and am a permanent resident in the United States. I currently reside in Gainesville, FL. A copy of my *curriculum vitae* is attached hereto as **Exhibit B**.

4. We have reviewed the Final Official Action (hereinafter, "the Action") dated May 22, 2006 issued by the U.S. Patent and Trademark Office (P.T.O.) charged with assessing the patentability of the captioned patent application. We have also reviewed the references cited in the present and prior Official Actions including *inter alia*:

Pritchard *et al.*, *J. ENDOCRINOL.*, 172:411-42, 2003, (hereinafter, "Pritchard");

Paterna *et al.*, *METHODS,* 28:208-218, 2002, (hereinafter, "Paterna");

Lasic, *TIBTECH,* 16:307-321, 1998, (hereinafter, "Lasic");

Dhillon *et al. MOLEC. THER.*, 4(2):139-145, (hereinafter, "Dhillon");

Kier *et al, EXP. NEUROL.* 160:313-316, 1999, (hereinafter, "Kier");

Russell et al., *U.S. PATENT 6,156,303*, (hereinafter, "Russell"); and

Bagnasco *et al.*, *Endocrinol.,* 143(11):4409-4421, (hereinafter, "Bagnasco").

5. We understand that on page 6 of the Action, the P.T.O. has taken the position that claims 1-7, 11, 12, 21, 24, and 26-30 would be obvious to one of skill in this field of study by combining the teachings of Pritchard and Paterna (the Action page 6).

6. We also understand that in the same Action, the Examiner further considers the claimed invention to be obvious of one of skill in the art when combining the Pritchard, Paterna, Dhillon, and/or Bagnasco references (the Action at pages 7-9).

7. Similarly, we understand that on page 9 of the Action, the P.T.O. has taken the position that the inventions encompassed by claims 1-9, 21, 26 and 27 would also have obvious to one of skill in this field of study when combining the teachings of Pritchard and Paterna and Lasic.

8. We further understand that on page 10 of the Action, the P.T.O. has taken the position that claims 1-7, 11, 12, 21-24, 26-28, and 30 would be obvious to one of skill in the art over Pritchard and Paterna, further in view of Keir.

9. From page 11 of the Action, we understand that the P.T.O. has taken the position that claims 1-8, 11, 12, 21-24, 26-28, and 30 would have been obvious to one of skill in the art at the time of our invention when combining the teachings of Pritchard and Paterna, further in view of Russell.

10. We also note that the P.T.O. has taken the position on page 13 of the Action that previously-added claims 31-40 would also have been obvious to one of skill in the art by combining the teachings of Pritchard and Paterna.

11. We further understand that on page 15 of the Action, the P.T.O. has taken the position that claims 31-40 would be obvious to one of skill in the art over Pritchard in view of Paterna, and further in view of the teachings of Dhillon and Bagnasco.

12. We disagree with the assessment that the Paterna or Pritchard references, either alone or in combination with each other, or with the additionally cited references of Dhillon, Bagnasco, Lasic, Kier, or Russell would render the presently claimed subject matter obvious to a scientist working in this field of research.

13. In response to the Action, we now provide this declaration to demonstrate that neither Paterna nor Bognasco is available as prior art under 35 U. S. C. § 102, since the present invention was made by us in the United States at least as early as the public availability of the Paterna and Bognasco references. Because neither reference is available as prior art under 35 U. S. C. § 102, neither reference is properly citable under 35 U. S. C. §103(a), and as such, all of the rejections under 35 U. S. C. § 103 citing Paterna and/or Bognasco are moot.

14. In support of this antedating affidavit, we provide the following documentary evidence:

15. According to the printed publication of Paterna, we understand that the reference was published in Volume 28 of the scientific journal *Methods* at pages 208-218 in 2002 (a copy of the cover page of the reference is attached hereto as **Exhibit C**).

16. According to the website of the publisher of this journal, Volume 28 of *Methods* was published in the October 2002 issue of the journal, a date which is less than one year before the April 11, 2003 priority date of the instant application. (A copy of the journal's website entry demonstrating that the earliest electronic availability of the reference was October 9, 2002 is attached hereto at **Exhibit D**).

17. According to the printed publication of Bagnasco, we understand that the reference was published in Volume 143, Number 11 of the scientific journal *Endocrinology* at pages 4409-4421 (a copy of the cover page of the reference is attached hereto as **Exhibit E**).

18. According to the website of the publisher of this journal, Volume 143, Number 11 of *Endocrinology* was published in November 2002, a date which is less than one year before the April 11, 2003 priority date of the instant application. (A copy of the journal's website entry demonstrating that the earliest availability of the reference was November 2002 is attached hereto at **Exhibit F**).

19. We are providing the present declaration and attached documentary evidence to demonstrate that the claimed invention was made in the United States prior to the

publication dates of both the October 9, 2002 Paterna reference, and the November 2002 Bagnasco reference.

20. Evidence of the fact that the invention claimed in the captioned patent application was made in the United States prior to October 9, 2002 is shown in the attached **Exhibits G and H** and described in the following paragraphs. The studies described in the following paragraphs were conducted in Gainesville, Florida, in the United States.

21. We jointly conceived of the claimed invention prior to October 9, 2002. Attached hereto as **Exhibit G** is a copy of a vector preparation log sheet signed by me, Gang Li, on a date prior to October 9, 2002, showing transfection and large-scale production of an rAAV vector comprising a POMC-encoding polynucleotide construct that was deposited in the University of Florida Vector Core Facility, located in the Powell Gene Therapy Center, in the Department of Molecular Genetics and Microbiology College of Medicine University of Florida. This genetic material was prepared and titered at the facility prior to October 9, 2002, and was stored in a laboratory freezer under appropriate conditions by us on a date prior to October 9, 2002.

22. We later jointly disclosed our invention to the Office of Technology Licensing (OTL) at The University of Florida Research Foundation, Inc., (UFRFI) in Gainesville, FL. Where we understand that on or about March 24, 2003, Mrs.

Monya A. Dunlap, an employee of the OTL at UFRFI, received our disclosure and assigned it an OTL internal file code of "UF#11178." Initial evidence of this is provided in **Exhibit H**, a copy of the original invention disclosure by us to the OTL.

23. We understand that on or about April 9, 2003, Mrs. Dunlap then assigned responsibility for the preparation and filing of the U.S. provisional application upon which the present application claims priority, to the University's outside counsel, Williams, Morgan and Amerson (WMA), in Houston, TX, where Dr. Mark D. Moore, a registered patent agent, worked diligently throughout the preparation of the application from the time of receipt of the disclosure through April 11, 2003, when the U.S. provisional patent application was filed with the PTO.

24. We further understand that on or about February 18, 2004, Ms. Noel Burmeister, an employee of the OTL at UFRFI, authorized the University's outside counsel, Dr. Mark D. Moore, to prepare and file a U.S. utility application based upon our invention, claiming priority to the provisional patent application filed April 11, 2003. We understand that Dr. Moore and employees of WMA worked diligently on the preparation of this utility patent application from such time until it was filed in the PTO on April 12, 2004.

25. From a time prior to October 9, 2002 to the present time, we have continued to work diligently on various embodiments of the invention as described and claimed in both our provisional patent application, and the captioned United States utility patent application.

26. We hereby declare that all statements made herein of our knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

Oct 9, 2006
Date

Philip J. Scarpace, Ph.D.

Oct 12, 2006
Date

Gang Li, Ph.D.

Exhibit A

Certificate of Service

I hereby certify that this correspondence is being filed with the U.S. Patent and Trademark Office via EFS-Web on 10/23, 2006.

Autrey Brown

Autrey Brown

Exhibit A

CURRICULUM VITAE 7/1/2006

NAME: PHILIP J. SCARPACE, Ph.D.

DATE OF BIRTH: January 4, 1948 **E-mail:** scarpace@ufl.edu

MARITAL STATUS: Married

ADDRESS: Department of Pharmacology and Therapeutics, PO Box 100267, University of Florida, Gainesville, FL 32610

PHONE: **BUS:** (352) 392-8435 **FAX:** (352) 392-9696 **HOME**: (352) 335-2820

EDUCATION:

1966-1970	California State University, San Jose, B.S., Physics (minor Chemistry). California State Scholarship; Cumulative Average 3.5 of 4.0. Member, Tau Delta Phi - Scholastic Honorary Fraternity.
1970-1974	University of Rochester, Ph.D. degree in Biophysics, School of Medicine, Thesis area: Membrane transport.

PROFESSIONAL EXPERIENCE:

1994 to present	Professor of Pharmacology and Therapeutics, University of Florida, Gainesville, Florida.
1987 to 2004	Research Director, Geriatric Research, Education and Clinical Center, Veterans Administration Medical Center, Gainesville, Florida.
1999 to 2004	Research Career Scientist, Veterans Administration Medical Center, Gainesville, Florida.
2000 to 2001	Acting Director, Geriatric Research, Education and Clinical Center, Veterans Administration Medical Center, Gainesville, Florida.
1987 to 1994	Associate Professor of Pharmacology and Therapeutics, University of Florida, Gainesville, Florida.
1988 to 1993	Associate Director, Center for Research on Oral Health and Aging, University of Florida, Gainesville, Florida.
1977-1987	Chief, Molecular Biophysics Laboratory, Geriatric Research, Education and Clinical Center, Veterans Administration Medical Center, Sepulveda, CA.
1977-1987	Assistant Research Professor, Dept. of Medicine, University of California School of Medicine, Los Angeles, California.
1979-1981	Assistant Professor of Mathematics, California State University at Northridge, California.
1977-1981	Instructor of Mathematics, (Computer Sciences), Moorpark College, Moorpark, California.
1975-1976	Fellow, Division of Endocrinology, Department of Medicine, University of California School of Medicine, San Diego, California.
1975-1976	Assistant Professor of Physiology, San Diego State University, San Diego, California.

PROFESSIONAL ACTIVITIES:

Member: American Society for Pharmacology and Experimental Therapeutics. North American Society for the Study of Obesity (fellow). Gerontological Society of America (fellow).
Program Chair, Gerontological Society of America Annual Meeting, 1993;
Secretary-Treasurer, Gerontological Society of America, Biological Sciences, 2000-2003.

VA Merit Review Board: 2001-2005
GRECC Review Panel: Reviews applications for new VA gerontological centers, 1991-2000.
NIH Study Section: Biochemical Endocrinology, Ad Hoc Study Section, 1990.
VA Merit Review Board: Ad Hoc Reviewer, 1984-1999.
VA Medical/Dental Fellowship: Ad Hoc reviewer, 1990.

Associate Editor: Growth, Development and Aging, 1988 - present.
Associate Editor: Journal of Gerontology: Biological Sciences, 1996 - 2000.
Editorial Review Board: American J of Physiology: Endocrinology & Metabolism 1998 - 2001.
Editorial Review Board: Journal of Gerontology: Biological Sciences, 1992 - 1996

Journal Referee: Endocrinology, Proceeding of the Society for Experimental Biology and Medicine, Molecular Pharmacology, Pediatric Research, Neuroendocrinology, Growth, J. of Gerontology, American J. of Physiology, J. of American Geriatric Society, J. Clinical Investigation, Life Sciences, and Mechanisms of Aging and Development, Metabolism.

Committees: Search Committee for GRECC Directors, Search Committees UF Faculty. GRECC Education Committee, Research and Development Committee, Chairman, Geriatric Research Committee. Sub-committee for Research Safety, Co-Chairman Animal Studies Committee (Sepulveda), Research and Development Committee (Sepulveda), Safety Committee (Sepulveda). Executive Committee, Gerontological Society of America.

Reviewer: Research and Development Committee, VAMC, Sepulveda, CA and VAMC Gainesville, FL.
University Affiliation: Department of Aging and Geriatric Research, Institute on Aging, Center for Neurobiology of Aging, Brain Institute.

CURRENT RESEARCH SUPPORT (direct cost):

2003-2006	Veterans Administration Type II Merit Review, co-investigator and mentor, (PI: Yi Zhang) "Role of the central melanocortin pathway in age-related obesity", $370,000.
2003-2007	National Institutes of Health (NIA), principal investigator, "Age-related obesity: Interventions with gene delivery", $1,000,000.
2003-2008	National Institutes of Health, co-investigator (PI: Sergei Zolotukhin) "rAAV-mediated metabolic engineering in vivo", $1,250,000.
2004-2009	National Institutes of Health (NIA), principal investigator, "Leptin resistance: one mechanism underlying age-related obesity", $1,250,000.
2006-2010	Veterans Administration Merit Review, co-PI, (PI: Yi Zhang), "Alleviating Age-Related Obesity: Intervention by POMC Gene Therapy", $870,000.

PAST COMPETITIVE RESEARCH SUPPORT:

2000-2005	Veterans Administration Merit Review, principal investigator, "Leptin: TNF-alpha and IL-6: Role in the increase in body weight with age", $626,000.
1999-2004	National Institutes of Health (NIA), principal investigator, "Impaired leptin responsiveness with age", $511,000.
2002-2003	Veterans Administration Type II Merit Review, co-investigator, "Role of leptin in blood pressure with age", $100,000.
1999-2003	Veterans Administration Merit Review, co-investigator (PI: Nihal Tumer), "Catecholamine Biosynthesis Pathways with Age", $429,000.
2000-2002	National Institutes of Health, co-investigator, "Cytokine Gene Therapy and Obesity", $210,000.
1998-1999	NIH RO3, co-principal investigator, "Beta-2-agonist restoration of muscle mass in aged rats", $50,000.
1997-2000	Veterans Administration Merit Review, principal investigator, "Leptin: Regulation by Sympathetic Activity and Role in Energy Expenditure", $300,000.
1995-1999	Veterans Administration Merit Review, co-investigator, "Age Related Changes in Tyrosine Hydroxylase in Adrenal Medulla", $252,000.
1994-1999	National Institutes of Health (NIA), principal investigator, "Brown Fat Thermogenesis: Response to Cold and Age", $506,000.
1992-1995	American Heart Association, principal investigator, "Plasticity of ß-Adrenergic Signal Transduction in Heart: Influence of Age and Exercise", $80,000.
1992-1993	University of Florida, principal investigator, "Atypical β_3-Adrenergic receptors: Unique Pattern of Desensitization", $9,000.
1990-1994	Veterans Administration Merit Review, principal investigator, "Pharmacology of Impaired Fever Response and Thermoregulation in Aging", $335,000.
1990-1991	University of Florida, principal investigator, "Impaired Febrile Response in Senescence", $5,000.
1988-1993	NIH Center for Research on Oral Health and Aging, Associate Director of Center, $2,500,000, principal investigator of one of four projects, "β-adrenergic Mechanism in Salivary Protein Secretions", $550,000.
1988-1989	University of Florida, principal investigator, "β-adrenergic Function in Senescence", $11,500.
1987-1990	Veterans Administration Merit Review, principal investigator, "β-adrenergic Function in Senescence: Influence of Catecholamines" $190,000.
1983-1987	Veterans Administration Merit Review, principal investigator, "Regulation of Lung β-adrenergic Function in Senescence" $210,000.
1980-1983	Veterans Administration Merit Review, principal investigator, "Lung β-adrenergic Adenylate Cyclase: Effects of Glucocorticoids and Aging" $135,000.
1980-1981	American Lung Association, principal investigator, "β-adrenergic Receptors and Asthma" $20,000.
1978-1980	Veterans Administration Merit Review Grants, co-investigator, "Aging and Myocardial Hormone Responsiveness", $64,000.
1974-1975	NIH Individual Postdoctoral Research Fellow, Department of Radiation Biology and Biophysics, University of Rochester, Rochester, New York.

INVITED SEMINARS AND SYMPOSIUMS

University of Washington, 1975
University of Rochester, 1977
University of Rochester, 1981
Vanderbilt University, 1982
St. Louis University, 1983
University of Washington, 1983
GRECC, American Lake, 1983
ASPET, 1984
University of Miami, 1985
University of Florida, 1985
California State Univ., Northridge, 1986
University of California, Davis, 1986
Duke University, 1986
National Institute on Aging, 1986
Medical College of Pennsylvania, 1987
Drug Therapy in the Elderly Symposium, 1988
Gerontological Society of America, 1989
University of South Florida, 1998
Gerontological Society of America, 1998
GRECC, St. Louis, 1990
Case Western University, 1990
Medical College of Pennsylvania, 1991
Musculoskeletal Disorders Symposium, 1991
American Aging Association, 1991
Gerontological Society of America, 1991
University of Miami, 1992
Texas Tech University, 1994
Int. Society for Heart Research, 1994
National Institute on Aging, 1994
Southeastern Pharmacology Society, 1994
Gerontological Society of America, 1994
Gerontological Society of America, 1995
Texas Tech University, 1997
Gerontological Society of America, 1997
University of Maryland, 1998
University of South Florida, 1998
International Thermoregulation symposium, 199
Gerontological Society of America, 1999
Serono Symposia: Endocrinology of aging, 1999
Gordon Conference: Biology of Aging, 2001
International Congress of Nutrition, 2000
IAMS Nutrition Symposium, 2000
N American Society Study of Obesity, 2001
International Congress of Nutrition, 2002
International Obesity Congress, 2002
Gerontological Society of America, 2002
Lilly, 2003
Nutrition and Aging XVIII, 2003
University of Texas, San Antonio, 2003
Gerontological Society of America, 2003
Endocrine Society, 2004
Gerontological Society of America, 2004
VA Research Day, 2005
International Congress of Physiology, 2005
Society for Ingestive Behavior, 2005

Symposium Chairman:

International Congress of Gerontology (1989)
Infections, Immunology and Aging (1989)
The Gerontological Society of America (1990)
Current Issues in Geriatric Dentistry (1990)
The Gerontological Society of America (1991)
The Gerontological Society of America (1993)
The Gerontological Society of America (1995)
The Gerontological Society of America (1998)
XI Int. Symposium of Thermoregulation (1999)
Gerontological Society of America, 2003
Gerontological Society of America, 2004

RESEARCH PAPERS:

1. Scarpace, P.J. and W.F. Neuman. Quantitation of Ca^{2+} fluxes in chick calvaria. Biochem Biophys Acta 323, 267-275, 1973.
2. Scarpace, P.J. and W.F. Neuman. The blood:bone equilibrium I. The active accumulation of K+ into the bone fluid. Calcif Tiss Res 20, 137-149, 1976.
3. Scarpace, P.J. and W.F. Neuman. The blood:bone equilibrium II. Evidence against a pump for calcium or phosphate. Calcif Tiss Res 20, 151-158, 1976.
4. Scarpace, P.J., W.F. Neuman and L.G. Raisz. Metabolism of radioiodinated salmon calcitonin in rats. Endocrinology 100, 1260-1267, 1977.
5. Scarpace, P.J. and L.J. Deftos. Preparation and immunological characteristics of biologically active radioiodinated human CT. Endocrinology 101, 1398-1405, 1977.
6. Scarpace, P.J., J.G. Parthemore and L.J. Deftos. The distribution of biological active and inactive radioiodinated human calcitonin in the rat. Endocrinology 103, 128-132, 1978.

7. Abrass, I.B. and P.J. Scarpace. Glucocorticoid regulation of myocardial beta-adrenergic receptors. Endocrinology 108, 977-980, 1981.
8. Scarpace, P.J. and I.B. Abrass. Thyroid hormone regulation of rat heart, lymphocyte and lung beta-adrenergic receptors. Endocrinology 108, 1007-1011, 1981.
9. Scarpace, P.J. and I.B. Abrass. Thyroid hormone regulation of beta-adrenergic receptor number in aging rats. Endocrinology 108, 1276-1278, 1981.
10. Abrass, I.B. and P.J. Scarpace. Human lymphocyte beta-adrenergic receptors are unaltered with age. J Gerontol 36, 298-301, 1981.
11. O'Connor, S.W., P.J. Scarpace and I.B. Abrass. Age-associated decrease of adenylate cyclase activity in rat myocardium. Mech Ageing Dev 16, 91-95, 1981.
12. Scarpace, P.J. and I.B. Abrass. Glucocorticoid regulation of lung beta-adrenergic receptors. Drug Development Res 2, 91-94, 1982.
13. Tashkin, D.P., M.E. Conolly, R. Deutsch, K.K. Hui, M. Littner, P.J. Scarpace, and I.B. Abrass. Subsensitization of beta-adrenoreceptors in airways and lymphocytes of healthy and asthmatic subjects. Am Rev Respir Dis 125, 185-193, 1982.
14. Abrass, I.B., J.L. Davis and P.J. Scarpace. Isoproterenol responsiveness and myocardial beta-adrenergic receptors in young and old rats. J Gerontol 37, 156-160, 1982.
15. Abrass, I.B. and P.J. Scarpace. Catalytic unit of adenylate cyclase: Reduced activity in aged human lymphocytes. J Clin Endocrinol Metab 55, 1026-1028, 1982.
16. Scarpace, P.J., M.R. Littner, D.P. Tashkin and I.B. Abrass. Lymphocyte beta-adrenergic refractoriness induced by theophylline or metaproterenol in healthy and asthmatic subjects. Life Sci 31, 1567-1573, 1982.
17. Scarpace, P.J. and I.B. Abrass. Desensitization of adenylate cyclase and down regulation of beta-adrenergic receptors following in vivo administration of beta-agonist. J Pharmacol Exp Ther 223, 327-331, 1982.
18. Scarpace, P.J., S.W. O'Connor and I.B. Abrass. Thermal lability of adenylate cyclase: mechanisms of stabilization. Life Sci 32, 817-824, 1983.
19. Scarpace, P.J. and I.B. Abrass. Decreased beta-adrenergic agonist affinity and adenylate cyclase activity in senescent rat lung. J Gerontol 38, 143-147, 1983.
20. O'Connor, S.W., P.J. Scarpace and I.B. Abrass. Age-associated decrease in the catalytic unit activity of rat myocardial adenylate cyclase. Mech Ageing Dev 21, 357-363, 1983.
21. O'Connor, S.W., P.J. Scarpace and I.B. Abrass. The effects of age and cholesterol on the rat lung beta-adrenergic system. Biochem Biophys Acta 778, 497-502, 1984.
22. Abrass, C.K., S.W. O'Connor, P.J. Scarpace, and I.B. Abrass. Characterization of the beta-adrenergic receptor of the rat peritoneal macrophage. J Immunol 135, 1338-1341, 1985.
23. Scarpace, P.J., S.W. O'Connor and I.B. Abrass. Cholesterol modulation of beta-adrenergic receptor characteristics. Biochem Biophys Acta 845, 520-525, 1985.
24. Scarpace, P.J., L.A. Baresi, D.A. Sanford and I.B. Abrass. Desensitization and resensitization of beta-adrenergic receptors in a smooth muscle cell line. Mol Pharmacol 13, 495-501, 1985.
25. Scarpace, P.J., S.W. O'Connor and I.B. Abrass. Temperature and Isoproterenol modulation of beta-adrenergic receptor characteristics. Life Sci 38, 309-316, 1986.
26. Scarpace, P.J. Decreased beta-adrenergic responsiveness during senescence. Federation Proc 45, 51-54, 1986.
27. Scarpace, P.J. and I.B. Abrass. Beta-adrenergic agonist mediated desensitization in senescent rats. Mech Ageing Dev 35, 255-264, 1986.
28. Scarpace, P.J. and H.J. Armbrech. Adenylate cyclase in senescence: Catecholamine and parathyroid hormone pathways. Rev Clin Basic Pharmacol 6, 105-118, 1987.
29. Scarpace, P.J. Characterization of beta-adrenergic receptors throughout the replicative life span of IMR-90 cells. J Cell Physiol 130, 163-168, 1987.

30. Scarpace, P.J. and B.P. Yu. Effect of diet restriction on rat lung beta-adrenergic receptors and adenylate cyclase activity. J Gerontol 42, 442-446, 1987.
31. Scarpace, P.J., L.A. Baresi and J.E. Morley. Modulation of receptors and adenylate cyclase activity during sucrose feeding, food deprivation, and cold exposure. Am J Physiol 253, E629-E635, 1987.
32. Mader, S.L., A.S. Robbins, L.Z. Ruberstein, M.L. Tuck and P.J. Scarpace. Effects of age and posture on lymphocyte and platelet adenylate cyclase activity. Clin Sci 74, 331-334, 1988.
33. Scarpace, P.J., A.D. Mooradian and J.E. Morley. Age-associated decrease in beta-adrenergic receptors and adenylate cyclase activity in rat brown adipose tissue. J Gerontol 43, B65-B70, 1988.
34. Scarpace, P.J. and I.B. Abrass. Alpha- and beta-adrenergic receptor function in the brain during senescence. Neurobiol Aging 9, 53-58 1988.
35. Mooradian, A.D., P.J. Scarpace and J.E. Morley. The effects of dietary zinc on beta-adrenergic receptor and post receptor function. Acta Endocrinol 119, 174-180, 1988.
36. Scarpace, P.J. and L.A. Baresi. Increased beta-adrenergic receptors in the light-density membrane fraction in lungs from senescent rats. J Gerontol 43, B163-B167, 1988.
37. Scarpace, P.J., L.A. Baresi and J.E. Morley. Glucocorticoids modulate beta-adrenoceptor subtypes and adenylate cyclase in brown fat. Am J Physiol 255, E153-E158, 1988.
38. Scarpace, P.J. Decreased receptor activation with age - can it be explained by desensitization. J Am Geriatr Soc 36, 1067-1071, 1988.
39. Rosenthal, M.J., J.E. Morley, J.F. Flood and P.J. Scarpace. Relationship between behavior motor response of mature and old mice and cerebellar beta adrenergic receptor density. Mech Ageing Dev 45, 231-238, 1988.
40. Scarpace, P.J. and B.S. Bender. Viral pneumonia attenuates adenylate cyclase but not beta-adrenergic receptors in mouse lung. Am Rev Respir Dis 140, 1602-1606, 1989.
41. Mooradian, A. and P.J. Scarpace. The response to isoproterenol-stimulated adenylate cyclase activity after administration of triiodothyronine is reduced in aged rats. Horm Metab Res 21, 587-642, 1989.
42. Scarpace, P.J. Forskolin activation of adenylate cyclase in rat myocardium with age: Effects of guanine nucleotide analogs. Mech Ageing Dev 52, 169-178, 1990.
43. Borst, S.E., N. Narang, F.T. Crews and P.J. Scarpace. Reduced $alpha_1$-adrenergic receptor-mediated inositide hydrolysis in cardiac atria of senescent rats. J Cardiovasc Pharmacol 16, 444-448, 1990.
44. Scarpace, P.J. and M. Matheny. The putative β-Adrenregic antagonist CGP-12177A activates adenylate cyclase in brown adipose tissue but not in heart. Eur J Pharmacol 183, 2164-2165, 1990.
45. Borst, S.E. and P.J. Scarpace. Reduced high affinity $Alpha_1$-adrenoceptors in liver of senescent rats: Implication of assessment at various temperatures. Br J Pharmcol 101, 650-654, 1990.
46. Borst, S.E. and P.J. Scarpace. $Alpha_1$-adrenergic stimulation of inositide hydrolysis in liver of senescent rats. Mech Aging Dev 56, 275-280, 1990.
47. Scarpace, P.J. and M. Matheny. Adenylate cyclase agonist properties of CGP-12177A in brown fat: Evidence for atypical β-adrenergic receptors. Am J Physiol 260, E226-E231, 1991.
48. Scarpace, P.J., N. Tümer, and S.L. Mader. Beta-adrenergic function in aging: Basic mechanisms and clinical implications. Drugs and Aging 1, 116-129, 1991.
49. Scarpace, P.J., B.S. Bender and S.E. Borst. *E. coli* peritonitis activates thermogenesis in brown adipose tissue: Relationship to fever. Can J. Physiol Pharmacol 69, 761-766, 1991.

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Exhibit B

Certificate of Service

I hereby certify that this correspondence is being filed with the U.S. Patent and Trademark Office via EFS-Web on 10/23, 2006.

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EDUCATION

1999-2003	**University of Florida College of Medicine** Gainesville, FL	PhD in Pharmacology
1995-1997	**Peking Union Medical College & Chinese Academy of Medical Sciences** Beijing, China	MD
1989-1995	**Zhejiang Medical University** Hangzhou, China	Bachelor of Medicine

PATENT AND PUBLICATIONS

Scarpace PJ and **Li G** (April 12, 2004) U.S. Patent Application Serial No. 10/822,613 Entitled "rAAV vector-based pro-opiomelanocortin compositions and methods of use"

Li G, Scarpace PJ (2006) Pro-opiomelanocortin overexpression in the hypothalamus precipitates diet-induced obesity and is associated with diminished responsiveness to the central melanocortin activation. *Diabetologia* (In preparation)

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Li G, Mobbs CV, Scarpace PJ (2003) Central pro-opiomelanocortin gene delivery results in hypophagia, reduced visceral adiposity, and improved insulin sensitivity in genetically obese Zucker rats. *Diabetes* 52:1951-1957

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HONORS AND AWARDS

Certification	USMLE Step 1: **99/255** (May 30, 2003) Step 2 CK: **99/271** (Oct. 8, 2004) **ECFMG Certification** (June 9, 2005)
2004	The animal study of POMC gene therapy for obesity and diabetes was featured at the University of Florida News Release.
2003	**Best Paper Award First Place** in the Division for Systems and Integrative Pharmacology of the American Society for Pharmacology and Experimental Therapeutics (ASPET) at Experimental Biology 2003
2001, 2003	**Graduate Student Travel Awards** for Experimental Biology 2001 and 2003 by ASPET
1996	**Best Paper Award Third Grade Prize** for the presentation of *Effect of antigen-activated $CD4^+$ T cells from normal individuals on the function of γδ T cells* at the International Advanced Immunology Course 1996, Beijing, China.
1996	**Peking Union Medical College Scholarship Second Prize**
1990-1995	**Zhejiang Medical University Scholarship First Prize**

RESEARCH AND CLINICAL EXPERIENCE

2003-present **Postdoctoral Research Associate, University of Florida College of Medicine**
(Philip Scarpace, PhD)
Conducting research projects of gene therapy for treating obesity and its complications. Investigating the role of the central melanocortin system in the homeostatic regulation of body weight.

2005.9-present **Extern, Shands at the University of Florida Department of Anesthesiology**

2004.9-2005.1 **Volunteer, Shands at the University of Florida's Emergency Department**

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2005-Present **American Diabetes Association**
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Student and Fellow Section

2000-present **American Society for Pharmacology and Experimental Therapeutics**
Student and Fellow Section

2000-present **Federation of American Societies for Experimental Biology**
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US Permanent resident
Hobbies include soccer, swimming, jogging, and tennis

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Methods 28 (2002) 208–218

METHODS

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Recombinant adeno-associated virus vector design and gene expression in the mammalian brain

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Accepted 15 July 2002

Abstract

Efficiency and stability of recombinant adeno-associated virus (rAAV)-mediated gene expression within the mammalian brain are determined by several factors. These include the dose of infectious particles, the purity of the vector stock, the serotype of rAAV, the route of administration, and the intrinsic properties, most notably the rAAV receptor density, of the targeted area. Furthermore, the choice of appropriate regulatory elements in rAAV vector design is of fundamental importance to achieve high-level sustained in vivo transcription and translation. This review summarizes the characteristics of various transcriptional and posttranscriptional regulatory elements, and highlights their influence on the expression performance of rAAV vectors in the mammalian brain.

Keywords: Adeno-associated virus; Serotype; Brain; Neuron; Glia; Expression cassette; Promoter; Woodchuck hepatitis virus posttranscriptional regulatory element; Bicistronic vector; Regulated gene expression

1. Introduction

Recombinant adeno-associated virus type 2 (rAAV-2) vectors have been widely investigated for gene transfer to neurons in several animal models of human neurodegenerative diseases, including Parkinson's disease (PD) [1–5], lysosomal storage diseases (LSD) [6–8], and amyotrophic lateral sclerosis (ALS) [9]. Recombinant AAV-2 vectors provoke no toxicity and, with the exception of a few reports [10,11], no immunological responses against the transduced cells or the vector-derived gene product have been observed, even after administration of high vector doses. Therefore, this type of viral vector has attracted considerable interest as a gene transfer vehicle. Furthermore, the lack of any viral genes, the ability to efficiently transduce postmitotic cells in the central and peripheral nervous systems, and the fact that no human disease has been associated with wild-type (wt) AAV-2 make rAAV-2 vectors a valuable and interesting alternative to other gene delivery systems.

Over the past few years, significant improvements in rAAV vector production have led to high-titer and clinical-grade pure rAAV vector stocks. Adenovirus (Ad) coinfection was replaced by Ad minigenome plasmids harboring all necessary helper functions for rAAV-2 vector production [12–15]. Furthermore, some groups combined AAV packaging and Ad helper functions on a single plasmid [16,17] (Fig. 1). Using these plasmids, wt-like replication-competent AAV-2 (rcAAV-2) were no longer detected in rAAV-2 vector stocks [16,18–20]. Concomitantly, purification schemes based on time-consuming cesium chloride (CsCl) gradient ultracentrifugation were replaced by iodixanol gradient ultracentrifugation and subsequent HPLC-based affinity chromatography, yielding rAAV-2 preparations with significantly increased infectivity (higher transducing units/overall particle ratios) [21–23].

Attempts to overcome the limited cloning capacity ($\leqslant$5 kb) exploited the unique feature of AAV-2 inverted terminal repeats (ITRs) to join two (or more) independent rAAV genomes by intermolecular recombination [24,25]. Recently, vectors derived from alternative AAV serotypes have emerged [26–30], and some of them were shown to have great potential for gene transfer to the

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Endocrinology 143(11):4409–4421

doi: 10.1210/en.2002-220505

Evidence for the Existence of Distinct Central Appetite, Energy Expenditure, and Ghrelin Stimulation Pathways as Revealed by Hypothalamic Site-Specific Leptin Gene Therapy

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To identify the specific hypothalamic sites in which leptin acts to decrease energy intake and/or increase energy expenditure, recombinant adeno-associated virus vector-encoding leptin was microinjected bilaterally into one of four hypothalamic sites in female rats. Leptin transgene expression in the ventromedial nucleus and paraventricular nucleus induced comparable decreases in daily food intake (FI; 18–20%) and body weight (BW; 26–29%), accompanied by drastic reductions in serum leptin (81–97%), insulin (92–93%), free fatty acids (35–36%), and normoglycemia. Leptin transgene expression in the arcuate nucleus (ARC) decreased BW gain (21%) and FI (11%) to a lesser range, but the metabolic hormones were suppressed to the same extent. Leptin transgene expression in the medial preoptic area (MPOA) decreased BW and metabolic hormones without decreasing FI. Finally, leptin transgene expression in all four sites augmented serum ghrelin and thermogenic energy expenditure, as shown by uncoupling protein-1 mRNA expression in brown adipose tissue. Proopiomelanocortin gene expression in the ARC was up-regulated by leptin expression in all four sites, but neuropeptide Y gene expression in the ARC was suppressed by leptin transgene expression in the ARC but not in the MPOA. Thus, whereas leptin expression in the paraventricular nucleus, ventromedial nucleus, or ARC suppresses adiposity and insulin by decreasing energy intake and increasing energy expenditure, in the MPOA it suppresses these variables by increasing energy expenditure alone. (*Endocrinology* 143: 4409–4421, 2002)

LEPTIN PRODUCED BY adipocytes and hypothalamus (1–4) controls the daily management of body weight (BW) homeostasis by restraining food intake (FI) and enhancing energy expenditure (5–7). A loss of leptin control on these two central mechanisms invariably results in uncontrolled energy intake leading to obesity and attendant metabolic disorders such as hyperleptinemia, hyperinsulinemia, and type 2 diabetes (5–8). Numerous studies now suggest that despite the presence of elevated circulating leptin levels, the progressive age-related and environmentally based increase in adiposity is due to leptin insufficiency in the hypothalamus rendered by defective transport of peripheral leptin across the blood brain barrier and/or suboptimal production of leptin locally in the hypothalamus (9–14).

Gene delivery *in vivo* to the central nervous system has been facilitated by the development of a nonimmunogenic and nonpathogenic recombinant adeno-associated virus (rAAV) vector (15, 16). The rAAV has advantages over other viral vector systems because of availability of stable, high-titer vector for long-term expression of target genes in nondividing cells (15–17). Consequently, leptin gene therapy offers a novel way to reinstate the hypothalamic leptin insufficiency responsible for the age-related and environmentally based abnormal weight gain and adiposity.

We recently developed a rAAV-vector encoding the leptin transgene (rAAV-lep) (18). A single intracerebroventricular (icv) injection of this vector inhibited weight gain and adiposity for long periods in rats of both sexes maintained either on regular rat chow or high-fat diet (10, 11, 19, 20). Interestingly, in association with suppressed weights, these rats displayed drastic reductions in serum leptin, insulin, and free fatty acids (FFAs) along with normoglycemia. In addition, icv rAAV-lep augmented thermogenic energy expenditure alone or along with decreased FI (10, 11, 19–22).

The physiologically active long form of the leptin receptor is expressed in various hypothalamic sites, and leptin administration to rodents activates c-Fos protein in groups of neurons in multiple hypothalamic sites (5, 23–27), suggesting that receptive elements in these sites play a role in regulating energy balance. Experimental results showed that microinjection of leptin into several hypothalamic sites decreased food intake (28, 29). These sites include the arcuate nucleus (ARC)-paraventricular nucleus (PVN) axis in which leptin receptors are expressed in neurons expressing the orexigenic peptides, neuropeptide Y (NPY), and agouti- related peptide (AgrP) and in proopiomelanocortin (POMC) neurons producing the anorexigenic peptide, α-MSH (5, 6, 30, 31).

We have now extended our icv leptin gene therapy studies to ascertain whether intracranial delivery of rAAV-lep in distinct hypothalamic sites would transduce leptin-trans-

Abbreviations: AgrP, Agouti-related peptide; ARC, arcuate nucleus; BAT, brown adipose tissue; BW, body weight; FFA, free fatty acid; FI, food intake; GFP, green fluorescence protein; icv, intracerebroventricular; ISH, *in situ* hybridization; MPOA, medial preoptic area; NPY, neuropeptide Y; PF, pair fed; POMC, proopiomelanocortin; PVN, paraventricular nucleus; rAAV, recombinant adeno-associated virus; rAAV-lep, rAAV-vector encoding the leptin transgene; ROD, relative OD; UCP1, uncoupling protein-1; VMN, ventromedial nucleus.

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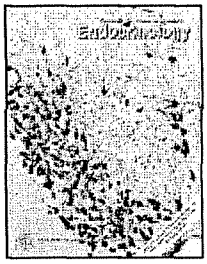

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Rapid Corticosteroid-Dependent Regulation of Mineralocorticoid Receptor Protein Expression in Rat Brain

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GRH-SOMATOSTATIN-GH:

GROWTH FACTORS-CYTOKINES-ONCOGENES:

INSULIN-GLUCAGON-GI PEPTIDES-DIABETES MELLITUS:

INTRACELLULAR SIGNAL SYSTEMS:

NEUROENDOCRINOLOGY:

Combined Blockade of Both μ- and κ-Opioid Receptors Prevents the Acute Orexigenic Action of *Agouti*-Related Protein
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Centrally Administered Neuromedin U Activates Neurosecretion and Induction of c-*fos* Messenger Ribonucleic Acid in the Paraventricular and Supraoptic Nuclei of Rat
Endocrinology 2002 143: 4320-4329, doi:10.1210/en.2002-220201 [Abstract] [Full Text]

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PTH-CALCITONIN-VITAMIN D-BONE: ◘

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Volume 28, Issue 2 , October 2002, Pages 208-218

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Recombinant adeno-associated virus vector design and gene expression in the mammalian brain

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Institute of Molecular Biology, University of Zurich, Winterthurerstrasse 190, 8057, Zurich, Switzerland

Accepted 15 July 2002. Available online 9 October 2002.

Abstract

Efficiency and stability of recombinant adeno-associated virus (rAAV)-mediated gene expression within the mammalian brain are determined by several factors. These include the dose of infectious particles, the purity of the vector stock, the serotype of rAAV, the route of administration, and the intrinsic properties, most notably the rAAV receptor density, of the targeted area. Furthermore, the choice of appropriate regulatory elements in rAAV vector design is of fundamental importance to achieve high-level sustained in vivo transcription and translation. This review summarizes the characteristics of various transcriptional and posttranscriptional regulatory elements, and highlights their influence on the expression performance of rAAV vectors in the mammalian brain.

Author Keywords: Adeno-associated virus; Serotype; Brain; Neuron; Glia; Expression cassette; Promoter; Woodchuck hepatitis virus posttranscriptional regulatory element; Bicistronic vector; Regulated gene expression

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Ref. #: 650

AAV PREP

Prepared for whom? _____ Amount requested ICF Date prep finished _____

FBS 5% DNA 2.72ml H2O 44.08ml

CaCl 5.2ml HBS 52ml Transfected by JF

rAAV (name) pCBA-PONC Lot # (transfection date) _____

rAAV plasmid lot # _____ rAAV plasmid (concentration by OD_{260}) 0.830 µg/µl

Amount of rAAV plasmid used in transfection 750 µl 622.5 µg

Helper plasmid pDG Helper plasmid lot # _____

Helper plasmid (concentration by OD_{260}) 0.950 µg/µl

Amount of helper plasmid used in transfection 1965.8 µl 1867.5 µg

Cell line/passage 293/P38 Confluency 61.6 %

Purification method Iod. band packed Heparin Processed by DW
(Iodixanol, CsCl, Heparin, FPLC)

Process Date _____

Desalted how? Spin Conc. w (0.1%) Rat Serum FINAL VOLUME ~500 µl
(Spin column, dialysis, ~~dilution~~)

Dot blot 4.26 x 10^11 /mL Date _____ By IK

rAAV titer by ICA 1.57 x 10^10 /mL Date _____ Titered by SR OUT

rAAV titer by GFP assay _____ Date _____ Titered by _____

wtAAV contamination by ICA _____

Particle infectivity ratio 27 Aliquot stored _____

Virus received by Guang Li _____ _____
Name Signature Date

General Comments: Titer < 5x10^10

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INVENTION DISCLOSURE

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1. Disclosure of Invention

An invention includes any discovery, new and useful process, composition of matter, article of manufacture, know-how, design, model, technological development, biological material, strain, variety, culture of any organism, or portion, modification translation, or extension of these items, and any mark used in connection with these items. Under patent law, this may include drugs, newly discovered, mutated or genetically engineered microorganisms or plants, new or altered forms of plant life, vaccines, cells, tissue and organ cultures, products of recombinant DNA research, hybrid cell cultures, processes involving microorganisms, monoclonal and polyclonal antibodies, engineered proteins, and some computer programs and designs.

A. **TITLE:** Reduction in food intake, adiposity, and body weight gain using peripherally administered recombinant Adeno-associated virus (rAAV) vector encoding Pro-opiomelanocrotin (POMC) cDNA.

B. **CONCISE DESCRIPTION OF THE INVENTION**

1. The disclosure should enable someone having knowledge of the field to understand the invention. Include essential elements (features, concepts, or new results of the invention, whichever is most applicable), their relationship to one another, and their mode of operation. Identify the elements that are considered novel.

A novel rAAV vector (Fig. 1) is described that is capable of reducing food intake, adiposity, and body weight gain and improving insulin sensitivity upon a single central (delivered bilaterally into hypothalamic arcuate nucleus) administration in rats that are obese, hyperphagic, and hyperinsulinemic.

The described rAAV encodes for the mouse Pro-opiomelanocrotin (POMC) cDNA under the control of CBA promoter. POMC is a pre-hormone, from which a family of peptides is derived including α-melanocyte stimulating hormone (α-MSH), β-MSH, γ-MSH, and adrenocorticotropic hormone (ACTH). These peptides, commonly know as Melanocortins are bioactive peptides involved in feeding and body weight regulation. To our knowledge, the described rAAV is the first vectors of this type capable of sustained reduction in food intake and body weight gain following bilaterally administration into the hypothalamic arcuate nucleus (Fig. 2 & 3). In addition, this vector improves insulin sensitivity and reduces serum cholesterol in these obese rats (Fig. 4) .

2. If the invention is an apparatus or system, attach drawings or a sketch and indicate if it has ever been built or tested. Use additional pages, attach drawings, manuscripts, papers, or other supporting material to facilitate understanding the invention. Attach any data which shows that the invention works.

Fig. 1 Diagram of rAAV vector plasmid. TR is AAV2 terminal repeat sequence; CBA promoter includes the CMV intermediate early enhancer sequence, the chicken β-actin promoter, non-coding sequence (Exon1) and intron from rabbit β-globin gene; the murine POMC; WPRE is the woodchuck hepatitis virus post-transcription regulatory sequence; bGH poly(A) is the bovine growth hormone polyadenylation sequence

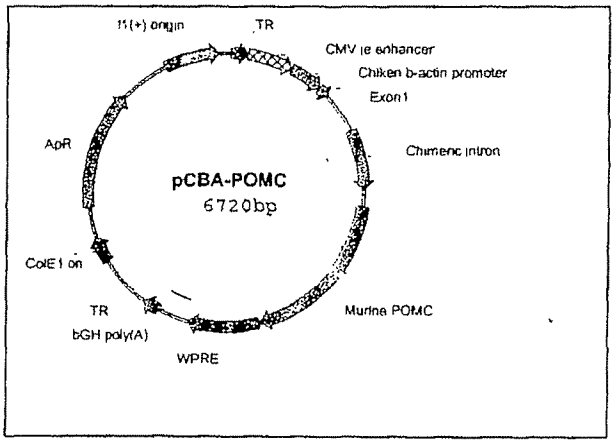


Fig. 2 Effect of rAAV-POMC vector injected bilaterally into hypothalamic arcuate nucleus on body weight gain of rats (n=6).

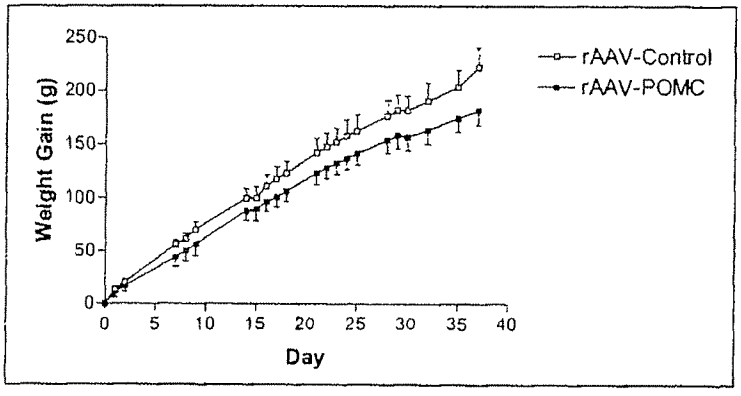


Fig. 3. Effect of rAAV-POMC vector injected bilaterally into hypothalamic arcuate nucleus on food intake of rats (n=6).

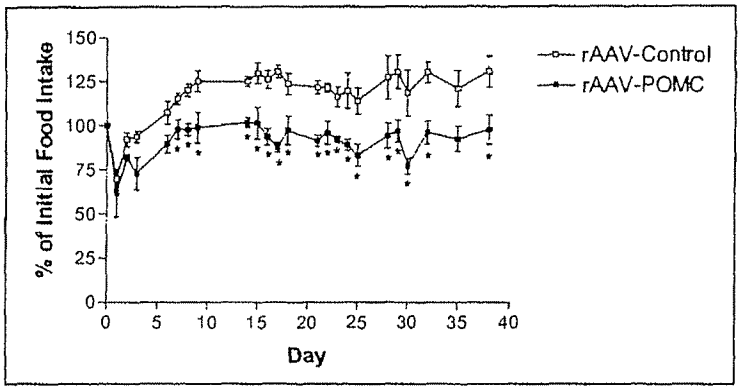
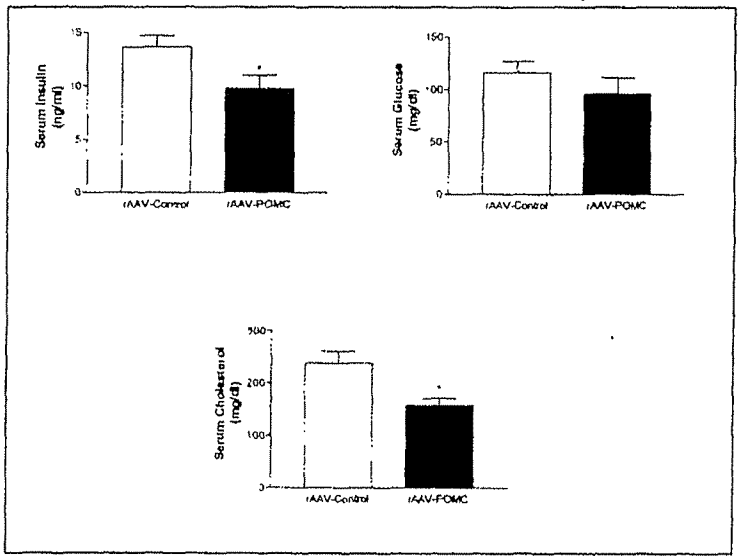


Fig. 4. Effect of rAAV-POMC vector injected bilaterally into hypothalamic arcuate nucleus on fasting serum insulin, glucose and cholesterol of rats (n=6).



B. **PRACTICAL FEATURES**: In lay terms, please describe the practical features of the invention.

The described vector could be used in human or animal clinic to curb the body weight gain, improve insulin sensitivity and reduce cholesterol levels in human obese patients or obese cats and dogs.

D. **PRODUCTS:** Describe the most likely products, services or commercial processes or other applications that could result from this invention (especially important if the invention is a chemical compound).

Gene therapy for obesity in humans or pets.

E. **BENEFITS**: Describe the primary benefits to a potential customer or user for any products, services, or commercial processes that might be developed from this technology (*e.g.*, what could it do to help a potential customer: lower expenses, increase productivity, efficiency or accuracy, minimize risk, simplify a process, overcome a defect, increase revenue, promote safety?).

Potential patients and pets would substantially decrease risk factors for atherosclerosis, hypertension, diabetes and other obesity-related disorders.

F. **What is the stage of development?**

___ Working prototype
_X_ Proof of concept
___ Analytical work

What work remains to complete development?

2. Market Information

Please provide this information to the best of your knowledge. We realize this information may not be readily known, but your input will be helpful.

A. Market Need

1. What is the ideal market for this technology? Who needs it?

>27% of US adults and 20-40% of cats and dogs are obese by current medical standards.

2. Why do you think the market needs this technology?

There is no working reliable drug to treat obesity efficiently in either humans or pets.

B. Market Demand

1. What factors influence demand in the market?

Social and economic.

2. Is demand becoming weaker or stronger?

Stronger.

C. Market Size

1. What is the estimated size of the market in annual dollars? $ _____

2. How did you derive this figure? Please attach any supporting data.

D. Market Research Information

1. Please list any published technical material such as patents, commercial literature, or scientific articles relating to the invention and any planned future publications.

- Li, G, C.V. Mobbs and P.J. Scarpace. Central Pro-melanocortin gene delivery results in hypophagia, reduced visceral adiposity and improved insulin sensitizity in genetically obese Zucker rats. Diabetes, (in review), 2003.

- Li G, C. Mobbs, and P.J. Scarpace. Central proopiomelanocortin gene delivery reduces food intake and visceral adiposity and improves insulin sensitivity in fa/fa Zucker rats. Abstract submitted for presentation at Experimental Biology, 2003.

2. Have you conducted any market research? If so, please list your sources.

No

E. Competing Products

1. What existing commercial products or services would this invention directly displace?

None exist.

2. What are the competing alternatives or substitutes?

Pharmacological treatment, physical exercise, dieting.

F. New Developments and Circumvention

1. Are you aware of any new developments (*e.g.*, technologies, products) by others to accomplish the same objective?

No.

2. How would you "get around" your own invention?

Don't know

G. **Suppliers**

1. What companies are the major suppliers for products or services that could or will compete with the invention?

Not known

2. Are there many suppliers or is the market dominated by few companies?

No companies provide such product

3. Would any of these suppliers be potential licensees?

N/a

H. **Competitive Advantages**

1. In comparison to currently existing products, services or processes, describe how the subject invention will provide or contribute to superior advantages or benefits.

One-time treatment delivers sustained weight-reducing effect.

I. **Regulatory Issues**

1. What are the regulatory or other entry barriers or impediments to the market?

3. Potential Licensees/Partners

A. If you are aware of a ***definitive*** licensee or a research sponsor who will license this invention, we must know immediately. Please indicate that company (with specific individual and phone number) in the space below:

_____

_____

B. Where would this invention have the most commercial value? Please indicate your evaluation by ranking the following geographic areas (1 being the highest).

United States	___1____	Japan	_____3____
Europe	___2____	Other (Please specify)	_____

C. **1.** Have you communicated with any industry representative regarding your invention?
YES _____ NO ___X____ If yes, please provide the following information:

Date of Disclosure	_____
Company	_____
Address	_____
City/State/Zip	_____
Telephone Number	_____
Individual Contact	_____
Official Title	_____

2. Was such a disclosure made under a confidentiality agreement? YES _____ NO ____

3. If yes to C.2, please provide a copy of that agreement.

D. Do you wish to license this invention for your own company? YES _____ NO __X___

Do you wish to discuss this possibility with OTL?

E. Do you wish to continue research on this invention if the entity licensing the invention provides funding? YES __X__ NO _____

4. Public Disclosure/Publication Plans

Public disclosure includes abstracts and presentations at scientific meetings (including poster sessions), public seminars, shelving of theses, publications, disclosure to others outside of the University who have not signed a confidentiality agreement, and the use, sale, or offer of sale of the invention. Identify dates and circumstances of any such disclosures. Also, indicate your future disclosure or publication plans, and NOTIFY the Office of Technology Licensing (address given in section 9) if the invention becomes publicly disclosed or published in the future (whether by plan or inadvertently).

A. Which of the following have you done or do you intend to do?

		YES	NO	DATE
1.	Publish	_X_	___	_Submitted_2/28/2003 to Diabetes_
2.	Oral Presentation	_X_	___	_2/21/02_Dept. of Pharmacology_
3.	Poster Session	_X_	___	_April 14, 2003_____
4.	Disclose to Industry Rep.	___	_X_	_____
5.	Other Public Dissemination	___	_X_	_____

5. Financial Support/Contract Identification

The primary purpose of this section is to identify any specific grant or contract number(s) (not the account number) and the external sponsors (governmental agencies, industrial sponsors, private agencies, or others) which provided support used to defray costs related to the research from which the invention resulted. This information is needed to determine whether this invention is subject to any commitments or restrictions arising from the terms of sponsorship. **(NOTE: The percentages indicated in B through E below must add up to 100%.)**

A. Name and address of the University facility, including any Agricultural Research and Development Center, where the invention was developed:

Name	University of Florida
Address	PO Box 100267 JHMHC
City, State, Zip	Gainesville, Fl 32610
Name	Dept of Veteran Affairs
Address	GRECC 182
City, State, Zip	Gainesville, Fl 32608

B. Please provide the following information regarding any contract and grant support of the invention process. (The following information must be provided for EACH contract or grant that supported the invention process; attach additional sheets if necessary.)

Name	NIH_____
Grant/Contract #	AG-17047
Address	_____
City, State, Zip	_____
P.I. Name	_Philip J Scarpace_____
Grant/Contract Title	Impaired leptin responsiveness with age.

What is the estimated the percentage of contribution through this contract/grant? _80%

C. Please provide the following information regarding any support for the invention process by the Florida Agricultural Experiment Station (FAES):

1. List Experiment Station (CRIS) Projects by number and title in effect during the research and development process:

USDA/CSRESS/FLA_____None_____

2. What is the estimated percentage of contribution through the FAES? __0__%

D. What is the University's estimated percentage of other support beyond any contracts, grants and/or support by FAES to the invention process? Support includes facilities, personnel, (including yourself) and supplies as well as money in the form of department, University, or gift funds. _____0_____%

E. What is the estimated percentage of other support? __20_____%
Please explain the circumstances of this support. (An example would be a co-contributor's independent funding from his or her institution.)

Dept of Veterans Affairs, Gainesville. Supported salary for Philip Scarpace and laboratory space and some equipment.

F. Did any of the contributors use any instrument(s) biological, chemical or physical material(s) or substance(s) obtained from others to create this invention? YES ___X___ NO _____

If YES, did a Materials Transfer Agreement or other document accompany the transfer?
YES _____ NO__X__ Please list any such agreements.

The POMC cDNA was a gift from Dr. Charles Mobbs, Mount Sinai Medical School, NY. The only document is an email agreement to provide us with the cDNA.

G. Did you or any of the co-contributors submit any University of Florida Disclosure of Outside Activities and Financial Interests, Reporting July 19__ - June 19__, Form # OAA-GA-L267-Rev. 3/98 for this year or the previous academic year?
YES ____ NO _ X___

(If YES, please provide copies of the approved University of Florida Disclosure of Outside Activities and Financial Interests, Form # OAA-GA-L267-Rev. 3/98, with this invention disclosure form.)

6. Identification of Contributor(s)

List below all persons who are believed to have contributed to the conception or reduction to practice of this invention. Please provide addresses and phone numbers where they may be contacted. Please make additional copies of this page if necessary.

Researcher # 1

First Name	Middle Name	Last Name
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Work Phone Number (352) 376-1611x6898	Home Phone Number (352) 335-2820
Work Fax Number (352) 374-6142	e-mail Address scarpace@ufl.edu
Citizenship US	

Researcher title and University affiliation, *e.g.*, Department, Center, College
Professor, Department of Pharmacology and Therapeutics

Researcher # 2

First Name	Middle Name	Last Name
Gang		**Li**

Work Address PO Box 100267 JHMHC	Home Address 370 Maguire Village Apt. 6
City, State, Zip, Country Gainesville, Fl 32610	City, State, Zip, Country Gainesville, Fl 32603
Work Phone Number (352) 376-1611x6951	Home Phone Number (352) 846-5790
Work Fax Number (352) 374-6142	e-mail Address ganglee2000@hotmail.com
Citizenship China	

Researcher title and University affiliation, *e.g.*, Department, Center, College
Graduate Student, Department of Pharmacology and Therapeutics

Note: The foregoing list should include names of all persons who may qualify as legal inventors. Inventorship is a legal question, which is generally determined by the attorney of record at the time a patent application is filed. A statement, which discusses the concept of inventorship, is available from the Office of Technology Licensing.

7. Signatures

Signature of researcher submitting disclosure:

Philip J. Scarpace

Name

Signature

3-20-05

Date

8. Distribution

Send the original and one copy of the completed disclosure to the Office of Technology Licensing, 308 Walker Hall, P.O. Box 115500, Gainesville, FL 32611, Telephone: (352) 392-8929.